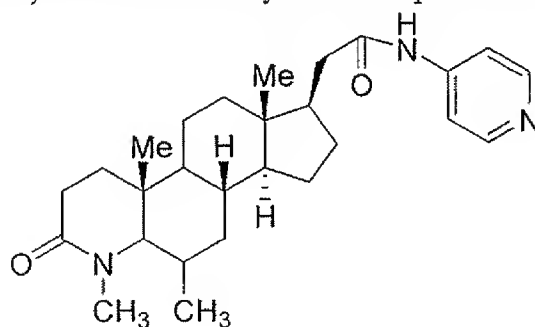


REMARKS

Claims 1, 5-11, 14-16, 19 and 32-40 are pending in this application. Claims 1, 5-11, 14-15, and 19-21 are rejected. Claim 16 is allowed. New claims 32-40 add no new matter and are supported by the original claims. Applicants point out that in claims 32-40, R4 cannot be an unsubstituted alkyl.

At paragraph 1 of the present Action, clarified the previous Action. The Examiner states:

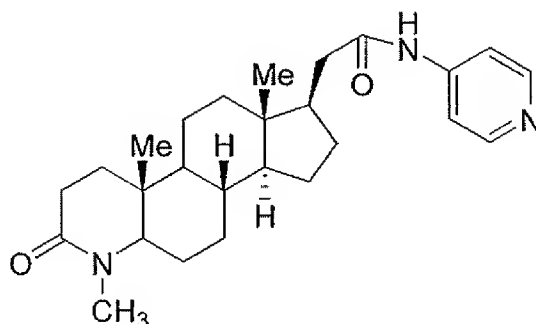
The Examiner would like to clarify that the chemical species elected by the Applicants in the reply filed on 3/10/2009 had R4=chloro. In the office action dated 6/10/2009, the Examiner indicated that the elected species was searched and found to be free of the prior art, and therefore, the search was expanded to other species of formula I, in which R4=methyl (see p. 4, section 2 of the office action dated 6/10/2009). This additionally searched species is shown below:



In the office action dated 6/10/2009, Claims 1-2, 5-11, 14-15, and 19-21 were rejected under 35 USC 103(a) as being unpatentable over Durette et al., US Patent No. 5,693,809 patent, in view of Audia et al., US Patent No. 5,670,514. However, in this office action, the Examiner erroneously referred to the US Patent No. 6,416,737, rather than US Patent No. 5,670,514. Therefore, this rejection will be properly restated, with reference to the US Patent No. 5,670,514, in this office action.

Applicants are most appreciative of the clarification.

Beginning at the middle of page 3, the Examiner argues that Durette '809, teaches a species the following species,



which differs from the previously depicted species only in that the Durette species teaches a hydrogen where applicants species possesses R4 = methyl and that hydrogen and methyl are homologues (which, by the way, applicants point out that they are not). The Examiner continues:

Homologues are expected to have similar chemical and physical properties, absent unexpected results. In response, the Applicants have submitted the reference Rasmusson et al., *J. Med. Chem.*, 29, pp. 2298-2315, (1986), and have argued that, as shown on pg. 2304, Table IV of this reference, the substitution of a methyl group for a hydrogen would not have been obvious, as this particular substitution on a steroid compound ring results in considerably different biological properties. While this argument has been fully considered, it is not found persuasive.

Applicants respectfully traverse. Applicants respectfully submit that the Examiner fails to appreciate the significance of the fact that a "homologue" rejection is based on a presumption, and that applicants can successfully rebut the rejection, by undercutting this presumption. As explained at MPEP 2144.09 V.

The presumption of obviousness based on a reference disclosing structurally similar compounds may be overcome where there is evidence showing there is no reasonable expectation of similar properties in structurally similar compounds. *In re May*, 574 F.2d, 1082, 197 USPQ 601 (CCPA 1978) (appellant produced sufficient

evidence to establish a substantial degree of unpredictability in the pertinent art area, and thereby rebutted the presumption that structurally similar compounds have similar properties); *In re Schechter*, 205 F.2d 185, 98 USPQ 144 (CCPA 1953). See also *Ex parte Blattner*, 2 USPQ2d 2047 (Bd. Pat. App. & Inter. 1987) (Claims directed to compounds containing a 7-membered ring were rejected as *prima facie* obvious over a reference which taught 5- and 6-membered ring homologs of the claimed compounds. The Board reversed the rejection because the prior art taught that the compounds containing a 5-membered ring possessed the opposite utility of the compounds containing the 6-membered ring, undermining the Examiner's asserted *prima facie* case arising from an expectation of similar results in the claims compounds which contain a 7-membered ring.).

In the present instance, the Examiner has made the presumption of like properties in compounds having R4 = hydrogen and compounds having R4 = methyl. As indicated by the Examiner this presumption is made merely on the basis that hydrogen and methyl are supposedly homologues. That is, the Examiner has presumed that **regardless of the position in question**, hydrogen and methyl have like properties.

The Examiner offers no data to show that the presumption is valid. On the other hand, applicants have countered the presumption with evidence that the presumption is not generally valid. That is, applicants have shown a position on the scaffold wherein the presumption is clearly not valid. Thus, the presumption is refuted and the rejection must be withdrawn.

Beginning at paragraph 7, the Examiner argues further that claims 1,5-11, 14-15 and 19-21 rejected as obvious under 35 USC 103(a) over Durette '809 in view of Audia. The characterization of Durette is substantially as mentioned above. The Examiner notes that that Durette '809 discloses that his compounds are 5- α reductase inhibitors but that the reference does not explicitly mention combining this disclosed compounds with alendronate. The Examiner continues that:

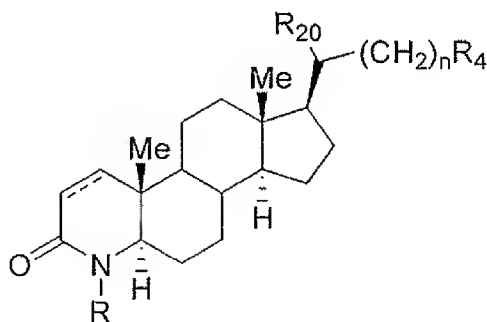
Audia et. al. teaches that bone loss can be reduced with 5- α reductase inhibitors inhibition (column 2, lines 32-3). Audia et. al. particularly

teaches that alendronate (as the sodium salt) is effective in reducing bone loss by inhibiting bone resorption (column 143, lines 37-50).

Applicants respectfully traverse. Given that only claims 20-21 include alendronate as a limitation, applicants presume that this rejection is directed only to those claims. In any event, as mentioned above, Durette '809 does not render applicants compound claims obvious. Accordingly, composition of matter claims comprising applicants non-obvious compounds are non-obvious. Nonetheless, in order to advance the prosecution in the case, applicants have cancelled claim 20-21. Applicants reserve the right to prosecute cancelled or unclaimed subject matter in a continuing or divisional application.

Beginning at paragraph 13, the Examiner rejects claims 1, 5-11 and 19 are rejected under 35 USC 103(a) as being unpatentable over Graham '051 in view of Audia. The Examiner states:

The claims are drawn to a compound of formula (I), as defined by the chemical structure shown below:



Graham et. al. teaches compounds of the same core structure as claimed compounds, with the following defined substituents of the formula shown above: R₂₀=H, or methyl; n=0; R₄=CONH-(Me)-pyridyl; R=Me or ethyl; a=single bond. These substituents correspond to the instantly claimed structure of formula (I) as follows:

R₁=methyl or ethyl; b=single bond; X=H; or methyl; R₂=methyl; R₄-pyridinyl (p. 3, line 15-p. 4, line 32; p. 31, compound 7a; p. 32, compounds 15a & 15b). The only difference between the compounds disclosed by Graham et. al. and the instantly claimed compounds is

that the R4 position for the claimed compounds is occupied by a methyl group, etc.; this position for the compounds taught by Graham et. al. is occupied by hydrogen. It is also known in the art that the substitution of a methyl group for hydrogen would be obvious, as they are considered homologues due to their structural similarity. The substitution of a methyl group of hydrogen on a known compound does not render the modification patentable, in the absence of unexpected or non-obvious results.

Applicants respectfully traverse. Given that only claims 20-21 include alendronate as a limitation, applicants presume that this rejection is directed only to those claims. In any event, the Graham reference possesses the same short-coming as Durette '809. As mentioned above, the applicants have provided substantial proof to refute the presumption that steroid core structures differing a methyl cannot be presumed to possess like properties. Accordingly, composition of matter claims comprising applicants non-obvious compounds are non-obvious. Nonetheless, in order to advance the prosecution in the case, applicants have cancelled claim 20-21.

Beginning at paragraph 14, the Examiner rejects claims 1-2 and 5-8 on the ground of obviousness type double patenting over US 7,482,357. In addition, at paragraph 16 of the Action, the Examiner provisionally rejects claims 1-2 and 5-8 on the ground of obviousness type double patenting over claims 1, 7 and 9-11 of US 10/557229.

Applicants respectfully traverse. Once again, the references possess the same shortcoming as Durette and Graham. Accordingly, for the reasons mentioned above, the Examiner must withdrawn the double patenting obviousness rejections.

Claims 1, 5-11, 14-15, and 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 refers to the functional groups defined for the R6 position. However, claim 1, as amended, no longer includes R6 as a substituent. Therefore, it is uncertain as to

what the claim limitations are. Claims 5-11, 14-15, and 19-21, which are dependent claims of Claim 1 or refer to claim 1, are rejected for this reason also.

In response, Applicants have amended the claims as indicated.

Finally, applicants point out that added claims 32-40 render all of the rejections moot.

Having addressed the outstanding issues, Applicants respectfully request early examination and allowance of the claims. The Examiner is invited to contact the undersigned attorney at the telephone number provided below if such would advance the prosecution of this application.

Respectfully submitted,

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